Message

From: Strynar, Mark [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5A9910D5B38E471497BD875FD329A20A-STRYNAR, MARK]
Sent: 9/28/2016 12:56:10 PM
To: Kenneke, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6439ff5240f04a5baf0b4f03f1a35aba-Kenneke, John]
CC: Medina-Vera, Myriam [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b081a1f48a044b4c9d1ebc4992c54dee-Medina-Vera, Myriam]
BCC: Lindstrom, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=04bf7cf26aa44ce29763fbc1c1b2338e-Lindstrom, Andrew]
Subject: RE: STICS: Clearance Initiation: #ORD-018614: Evaluation of the Immunomodulatory Effects of 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate ("GenX") in C57BL/6 Mice
Attachments: Strynar et al., 2015 ES&T.pdf; Dewitt et al., 2008 .pdf

Sure John,

We published a paper last year where we identified novel compounds in the Cape Fear river (Strynar et al., 2015). One of the compounds we have discovered in the river was the compound called GenX (2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate). This is a compound that has been made to replace PFOA as a surfactant in the process of making PTFE (Teflon) by certain manufacturers.

Formerly Jamie Dewitt (East Carolina University) was a post doc in NHEERL that worked with Bob Luebke and did immunotoxicology of PFOA in dosed rodent models collaboratively with me (Dewitt et all,2009). After having some discussions with Jamie it became apparent there was no toxicological data on this new compound and there appeared to be no high throughput toxicological assay for immunotoxicology. She offered to replicate the study we did on PFOA with this new compound GenX in a collaborative effort. I supplied the chemical and did analysis of dosed rodent serum/urine and she performed the dosed rodent studies.

I think in the future as it relates to CSS we should have a mechanism for inclusion of newly discovered compounds into our NCCT battery of assay to see what we can understand about compounds with no known tox data. I have already been approached by the NTP (Fenton and DeVitto) about inclusion of some of these compounds I have discovered in their tox assays after they read my paper.

Let me know if you need more.

Mark

From: Kenneke, John
Sent: Wednesday, September 28, 2016 8:38 AM
To: Strynar, Mark <Strynar.Mark@epa.gov>
Cc: Medina-Vera, Myriam <Medina-Vera.Myriam@epa.gov>
Subject: FW: STICS: Clearance Initiation: #ORD-018614: Evaluation of the Immunomodulatory Effects of 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate ("GenX") in C57BL/6 Mice

Hi Mark,

I would appreciate it if you could send me some additional details on the paper below; Tina would be interested in learning more about it. I do not need anything extensive. Maybe some background information on the nexus for the work, specific areas of CSS program you think this work will benefit, future direction of work, etc. Thanks.

John

From: ORD_STICS@epa.gov [mailto:ORD_STICS@epa.gov]
Sent: Tuesday, September 27, 2016 2:59 PM
To: Cowden, John <Cowden.John@epa.gov>; McMahen.Rebecca@epa.gov; Linnenbrink, Monica <Linnenbrink.Monica@epa.gov>; Strynar, Mark <Strynar.Mark@epa.gov>; Matney, Rachel <Matney.Rachel@epa.gov>; Franzosa, Jill <Franzosa.Jill@epa.gov>; Zukowski, Benjamin <Zukowski.Benjamin@epa.gov>; Loughran, Michael <Loughran.Michael@epa.gov>; Bahadori, Tina <Bahadori.Tina@epa.gov>; Kenneke, John <Kenneke.John@epa.gov>; Buckley, Timothy <Buckley.Timothy@epa.gov>; Tong-Argao, Sania <Tong-Argao.Sania@epa.gov>; Vazquez, Margie <Vazquez.Margie@epa.gov>
Subject: STICS: Clearance Initiation: #ORD-018614: Evaluation of the Immunomodulatory Effects of 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate ("GenX") in C57BL/6 Mice

This e-mail is to inform you that you have been copied on the following Chemical Safety for Sustainability clearance submission in STICS:

- **Product type, subtype:** Journal Article, Peer Reviewed
- **Product title:** Evaluation of the Immunomodulatory Effects of 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate ("GenX") in C57BL/6 Mice
- **Author(s):** Rushing, B,Q. Hu,J. Franklin,R. McMahen,S. Dagnino,C. Higgins,M. Strynar and J. DeWitt
- **Initiator:** Jan Contreras,ord/nerl/emmd
- **ORD Tracking Number:** Tracking # ORD-018614

- **Product Description / Abstract:** 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate, known as "GenX" by its U.S. manufacturer, is a compound designed to replace perfluorooctanoic acid (PFOA), a perfluoroalkyl compound that has been mostly phased out of U.S. production due to environmental persistence, detectable serum concentrations in humans and wildlife, and reports of systemic toxicity. In experimental rodent models, PFOA exposure suppresses T cell-dependent antibody responses (TDAR) and has been reported to suppress vaccine responses in exposed humans. To determine if this replacement compound also modulates TDAR and related parameters, male and female C57BL/6 mice were exposed to 0, 1, 10, or 100 mg/kg per day by gavage for 28 days. Serum and urine were collected at various times after the initial dose to determine test compound concentrations. Following immunization with sheep red blood cells (SRBCs) on day 24, SRBC-specific IgM antibody responses and splenic lymphocyte subpopulations were evaluated five days later. Body weight did not differ by dose, but relative liver weight was increased in both sexes at 10 and 100 mg/kg. SRBC-specific IgM antibody production was suppressed in female animals exposed to 100 mg/kg. No changes in splenic T lymphocytes were observed for either sex, but the percentage of B lymphocytes was reduced at 1 and 100 mg/kg in male animals, which has not previously been observed in animals exposed to PFOA or PFOS. Additionally, serum concentrations were maximized after only five days of dosing, females had less serum accumulation and higher serum clearance than males, and males had higher concentrations than females in urine at all time points and doses. While this PFOA-replacement compound appears to be less potent at suppressing TDAR relative to PFOA, further studies are necessary to determine its full immunomodulatory profile and its potential synergism with other per- and polyfluoroalkyl substances of environmental concern.

- **Tracking and Planning**
  - Task ID: CSS16.02.01
  - Task: RMS Rapid Exposure and Dose Task

- Product Title: N/A - Not Applicable
- Product Description: N/A - Not Applicable
- Project: Rapid Exposure and Dose
- Topic: Chemical Evaluation
- Research Program Area: Chemical Safety for Sustainability

- **HISA? ISI? High Profile?:** Not Applicable
- **QA form attached in STICS?:** Yes
- **QAPP Reference:** QAPP for the biomarkers methods development laboratory
- **Keywords:**
  - PFOA
  - PFOS
  - undecafluoro-2-methyl-3-oxahexanoic acid
  - genX

- **Journal Name:** ENVIRONMENTAL TOXICOLOGY

This submission can be found in your In Progress tab. Please click here to access STICS.